

Application of Tolerogenic Dendritic Cells for Hematopoietic Stem Cell Transplantation

Grant Award Details

Application of Tolerogenic Dendritic Cells for Hematopoietic Stem Cell Transplantation

Grant Type: Transplantation Immunology

Grant Number: RM1-01710

Project Objective: Objective of this two year grant is to investigate the role of tolerogenic dendritic cells in inducing tolerance for hematopoietic stem cell transplantation.

Investigator:

Name:	Husein Hadeiba
Institution:	Palo Alto Veterans Institute for Research
Type:	PI

Disease Focus: Immune Disease

Human Stem Cell Use: Adult Stem Cell

Award Value: \$733,061

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 2 + NCE (new end 12/31/12)

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Grant Application Details

Application Title: Application of Tolerogenic Dendritic Cells for Hematopoietic Stem Cell Transplantation

Public Abstract:

The immune system protects us from invading pathogens, but has to be kept in check to prevent harmful responses to our own tissues. Unique immune "suppressor" cells have been recently characterized that prevent harmful responses to our own cells and proteins. We have recently identified unique populations of white blood cells, called dendritic cells that can induce the development of such "suppressor" cells. More importantly these immunosuppressive dendritic cells are unique in that they have special molecules on their cell surface that target them to tissues in the body where autoaggressive immune cells are either killed off or shut down during the development of the immune system.

We wish to (i) expand and isolate populations of dendritic cells based on their cell surface expression of these special trafficking molecules and then (ii) use them as facilitator cells in transplants of stem cells from a foreign donor. The idea behind our approach in stem cell transplantation therapy is that immunosuppressive dendritic cells from donor A will educate the immune system in recipient B to recognize cells and proteins from the donor as self and not to mount destructive rejection responses to stem cell grafts from the same donor (A).

Finally we wish to use a preservation protocol in formalin-based solvents to maintain the immunosuppressive attributes of these dendritic cells forever. That way they can be safely administered to patients that receive mismatched stem cell grafts without ever worrying that the function of these dendritic cells will change after injection into the patient. We will work to establish protocols for the use of immunosuppressive dendritic cells as facilitator cells for foreign stem cell grafts in the clinic.

Statement of Benefit to California:

The use of stem cell grafts has been pioneered in the clinics and biotech labs (e.g. Geron) of California and has been a therapy of choice for the replacement of diseased tissue in many patients. With the ban lifted on embryonic stem cell research, we will see more patients throughout California embracing this form of therapy. However rejection of foreign tissue grafts, including stem cells, has challenged researchers and clinicians to understand the cellular and molecular mechanisms responsible for immune-mediated rejection of foreign grafts. The preliminary results from studies described in this proposal suggest that the host immune system can be educated to recognize foreign stem cell grafts as "self" if the host is first pre-conditioned with facilitator cells obtained from the donor. The studies described in this proposal seek to identify potent facilitator cells for use in transplant therapy. This approach will allow patients throughout California that suffer from ailments that involve diseased tissue, from neurodegenerative and autoimmune disorders to immune cell cancers, to receive foreign stem cell grafts without the complications of graft rejection.

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